



Docket PHO-120

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Dees et al.

Serial No.: 09/817,448

Filed: March 26, 2001

For: Intracorporeal Medicaments for High
Energy Phototherapeutic Treatment
of Disease

Examiner: G. Gabel

Art Unit: 1641

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Shannon Wallace

February 23, 2006

AFFIDAVIT OF AMOS NORMAN UNDER 37 CFR §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Amos Norman, do hereby state:

1. I have a Ph.D. degree in biophysics from Columbia University in New York City. My career has been in the Department of Radiation Oncology, Geffen School of Medicine, University of California, Los Angeles, where I am currently Professor Emeritus. I have published some two hundred articles in refereed journals on research in radiation physics and radiation biology, taught courses in radiation physics, health physics and related topics to graduate students in our Biomedical Physics Program, undergraduates and Residents in Radiology and Radiation Oncology; and served for many years as a member and chair of the UCLA Radiation Safety Committee. I am a Fellow of the American College of Radiology and the American

Association of Physicists in Medicine (AAPM) and received the AAPM Lifetime Achievement Award. I am also the lead inventor of U.S. Patent 5,008,907, which relates to radiation therapy and apparatus for use in delivering therapeutic doses of x-rays for radiation therapy.

2. I am familiar with the 09/817,448 application as I was provided with and reviewed the specification and drawings for this application.

3. I was also provided with and reviewed pages 19-23 of Applicants' response of June 3, 2005 in the '448 application. As explained below, I agree with the statements in this prior response.

4. The '448 application lists a number of halogenated xanthenes, including Rose Bengal, for inclusion in the compositions of the invention of the application. I am familiar with Rose Bengal and the related halogenated xanthenes having a molecular weight less than that of Rose Bengal.

5. No one knowledgeable about radiation therapy, radiation biology or radiation chemistry would mistake Rose Bengal or the other compounds listed in the '448 application as containing radioactive atoms and thus being radioactive. One knowledgeable in the field also would know that these compounds, or any radiosensitizer composition containing these compounds, do not contain a radioisotope.

6. As explained in the points below, the disclosure in the '448 application supports what is well known to those in the field, including the following statements:

- a. the therapeutic performance of a radiosensitizer is a function of enhanced absorption of an applied radiation dose in sensitized tissues relative to that in non-sensitized tissues (PHO-120 Specification, p. 3);
- b. differential absorption may be achieved by use of radiosensitizers having a high absorption cross-section for a particular type of radiation (pp. 3-4); and
- c. radiosensitizers must also have low toxicity in the absence of applied ionizing radiation (p. 4).

7. It is common knowledge in the field that radiosensitizers function by working in conjunction with separately applied ionizing radiation and would not be radioactive themselves. It would be counterproductive for radiosensitizers to be radioactive because such a hypothetical radioactive radiosensitizer would be intrinsically toxic.

8. It is important for radiosensitizers to be non-toxic in the absence of applied radiation because this allows the interventional radiologist to selectively deliver the therapeutic radiation doses to the diseased tissue being treated while avoiding harm to other tissues.

9. Rose Bengal and the other halogenated xanthenes listed in the '448 application are shown to be not toxic to cells or tissues in the absence of applied ionizing radiation, and must be non-radioactive. Since they are non-radioactive, they also must not contain any radioisotopes.

10. I have reviewed the molecular weights (mw) listed in Table 1 of the '448 application for the halogenated xanthenes and deem that they exclude all radioisotopes, since such radioactive analogs would have different molecular weights than those listed. One knowledgeable in the field would know upon inspection of the listed molecular weights in Table 1, that those halogenated xanthenes exclude incorporation of a single radioisotope.

11. I have reviewed the molecular structures shown in Figures 1a and 1b in the '448 application and deem that they do not indicate the presence of a radioisotope in the structure of the halogenated xanthenes.

12. Further, when the chemical formula or name of a radiolabeled molecule is written, it is convention to clearly designate the existence of all radioisotope in such formula or name. The absence of such designation in the chemical names used throughout the '448 application would convey to one knowledgeable in the field that the present application excludes incorporation of radioisotopes in the named halogenated xanthenes.

Based upon information and belief, I declare under the penalty of perjury that the foregoing is true and correct.

Amos Norman
Professor Amos Norman, Ph.D.

Date: 9 Jan 2006